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Helge Zieler

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EXAMINER

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/590,546	Applicant(s) ZIELER ET AL.	
	Examiner BRENT PAGE	Art Unit 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 July 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) See Continuation Sheet is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) See Continuation Sheet is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 22 August 2006 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>2/2008</u> . | 6) <input type="checkbox"/> Other: _____ |

Continuation of Disposition of Claims: Claims pending in the application are 1-3,6,7,10,11,14-16,19,25,30,39,40,43-46,54,56-63,66,67,76,77,82-87,89,90,93 and 96.

Continuation of Disposition of Claims: Claims rejected are 1-3,6,7,10,11,14-16,19,25,30,39,40,43-46,54,56-63,66,67,76,77,82-87,89,90,93 and 96.

DETAILED ACTION

Claims 1-3,6,7,10,11,14-16,19,25,30,39,40,43-46,54,56-63,66,67,76,77,82-87,89,90,93 and 96 appear to be pending. Claim 6 is not in the current claim listing and depends from a cancelled claim. Clarification is requested as to claim 6 status.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. There are 4 hyperlinks embedded in paragraphs 83, 111, and 210 (2 hyperlinks) of the specification, respectively. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Drawings

The drawings are objected to because they contain nucleic acid sequences without the corresponding SEQ ID NOs in either the figure itself or in the Brief Description of Drawings section of the specification. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief

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description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112-2nd paragraph

Claim 6 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6 recites the limitation "the plant according to claim 5" in line 1. There is insufficient antecedent basis for this limitation in the claim because claim 5 is currently cancelled. Because the claim contains indefinite limitations based on a cancelled claim, the claim can not be examined in its current form. Clarification of the claim status as being amended or cancelled is required.

Claim Rejections - 35 USC § 112-scope of enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 7, 10-11, 14-16, 19, 25, 30, 39-40, 43-46, 54, 56-63, 66-67, 76-77, 82-87, 89-90, 93 and 96 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for specific minichromosomes with defined sequence content based on species specific centromere repeats, does not reasonably provide enablement for any minichromosome of any size with any DNA content from any species of any kingdom as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are drawn to a plant comprising any minichromosome of any size below 1000 kilobases comprising any centromeric repeat in any copy number from any crop plant centromere.

In contrast, the specification provides guidance for specific BAC clones containing specific arrangements of known centromere repeats for use as centromeric DNA, specific telomeric repeats, and specific origin of replication sequences for function

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as a minichromosome. The specification does not give guidance for any minichromosome with any DNA composition as broadly claimed, not does the specification indicate which sequences are absolutely required for centromere function, telomere function or origin of replication function to enable one of skill in the art over the full scope of the claims. For example, no centromere contributions under about 50kb in length are shown to function as centromeres in a minichromosome in a plant cell.

Additionally, due to the claims broadly being drawn to any minichromosome from any source comprising any centromere, the claims read on multitudes of minichromosomes comprising multitudes of sequences from any species. Chromosome structure of animals is different than that of plants. Avramova (2002 Plant Physiology 129:40-49) discusses the heterochromatin of animals and plants. In plants, heterochromatin is located at the nuclear organizer and at the knobs, while in animals the heterochromatin is found in the telomeres, centromeres, and pericentric regions of the chromosome. Furthermore, there are no similar proteins to those known in animals to be associated with heterochromatin. (see page 41 second column third paragraph, for example).

Satellite DNA in mammals is different than that of satellite DNA in plants. In animals and yeast, satellite DNA is AT-rich while in plants, satellite DNA tends to be GC-rich (Fert et al in Buchanin et al 2000 Biochemistry and Molecular Biology of Plants, American Society of Plant Physiologists, Rockville, MD 20855, page 324). This basic difference in satellite DNA content would make the functioning of animal satellite DNA in plants as part of an artificial chromosome unpredictable.

Furthermore, the claims are drawn to minichromosomes wherein the only functional element recited other than structural genes is a centromeric sequence. Centromeric sequences are insufficient to maintain minichromosomes. Harrington et al (1997 Nature Genetics, 15:345-354 submitted by Applicant) teach that the sole presence of artificial centromeres, comprised of repeating sequence units, was insufficient to cause the segregation to daughter cells of minichromosomes containing them (see, e.g., page 346, column 2, bottom paragraph; page 347, paragraph bridging the columns and Table 1; page 348, column 1 top paragraph). Thus, claims drawn to transmissible plant centromeres which are comprised solely of repeating sequences, (as evidenced by discussion of minichromosomes in the specification wherein telomere sequences and origins of replication are discussed as “optional” sequences) are not enabled.

The function of a centromeric region is also unpredictable. Hall et al (2004 Current Opinion in Plant Biology 7:108-114) in a comprehensive review of plant centromeres discuss the field of plant centromeres and point out that although studies implicate satellites and retro-elements as important DNA sequences for centromere function, potential roles for other sequences have not been ruled out (see page 112, 3rd paragraph, for example). Claim 7 is broadly drawn to a minichromosome that is about 1000kb or less. There is no lower limit for size and therefore no limitation on the minimal size or minimal number of repeats for a functioning centromeric sequence. Absent guidance as to how many copies of the centromeric sequence are needed for centromere function, It would be undue experimentation for one of skill in the art

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evaluate all possible centromeric sequences and copy number combinations to evaluate them for centromeric function as broadly claimed.

Another required element of a functioning mini-chromosome, the DNA component necessary for an origin of replication in plants, is unpredictable in function. In a review of Origins and complexes, Bryant et al (2001 Journal of Experimental Biology 52:193-202) discuss the features and sequences of an origin of replication in plants. Bryant et al disclose that very few replication origins have been isolated from multicellular eukaryotes, and that most attempts to identify putative replication origins have relied on identifying ARS elements (see page 194, second full paragraph). Bryant et al disclose that such elements are unpredictable in the functioning of an origin in plants, and merely identify the ability of the sequences to function in yeast. Bryant et al state "The presence of budding yeast-type ARS elements in plant DNA does not therefore show that these elements are involved in replication origin in plants. Indeed, recent studies on origins of replication in the fission yeast *Schizosaccharomyces pombe* have indicated that *S. cerevisiae* may be a poor model for the structure of eukaryotic replication origins" (see page 194, second column, upper third of first full paragraph). Bryant et al further state "Understanding of the structure of plant DNA replication origins is further complicated by the findings that origin-to-origin spacing may vary in plant development, or in response to nutrients or hormones or to experimental manipulation" (see page 195 beginning of second paragraph). Bryant et al further disclose that nucleosome spacing and chromosome structure may be important for determining

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whether or not an origin is active (see page 195 second column end of first paragraph, for example).

Given the disclosures above and the lack of guidance as discussed above, it would be undue experimentation for one of skill in the art to evaluate each sequence component of a minichromosome, and further, each embodiment of the minichromosome, for function and stability as broadly claimed.

Claim Rejections - 35 USC § 112-written description

Claims 1-3, 7, 10-11, 14-16, 19, 25, 30, 39-40, 43-46, 54, 56-63, 66-67, 76-77, 82-87, 89-90, 93 and 96 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a plant comprising a minichromosome constructed from any DNA content, from any species including animal, insect or fungal, or any crop plant species (see claim 11), wherein the host may be any species relative to the minichromosome species of origin. This represents literally millions of embodiments and countless combination possibilities.

In contrast, the specification only describes the construction of brassica, tomato, soybean, tobacco, and maize-derived mini-chromosomes, and only describes the aforementioned species as host plants for the respective minichromosomes. The

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described examples are not deemed to be a representative number of working examples given the large, nearly unlimited genus claimed, particularly wherein the claims (other than claim 11) encompass mammalian, insect, and fungal species in addition to plant species for minichromosome generation. Absent a representative number of examples, the specification must describe the structures required for the claimed function (i.e. minichromosome activity). In the instant case, the specification describes species-specific sequences that are required for both centromere and minichromosome function, however, the specification does not describe the core sequences that would be required to isolate centromeres and construct minichromosomes from any species other than the exemplified species in the specification. Accordingly, the claims lack adequate written description over the full scope of the claims.

The Federal Circuit has recently clarified the application of the written description requirement. The court stated that a written description of an invention “requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials.” *University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1568; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The court also concluded that “naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material.” *Id.* Further, the court held that to adequately describe a claimed genus, Patent Owner must describe a representative number of the species of the claimed

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genus, and that one of skill in the art should be able to "visualize or recognize the identity of the members of the genus." *Id.*

Finally, the court held:

A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. *Id.*

See also MPEP section 2163, page 174 of chapter 2100 of the August 2005 version, column 1, bottom paragraph, where it is taught that

[T]he claimed invention as a whole may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence.

See also *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at 1021, (Fed. Cir. 1991) where it is taught that a gene (which includes a promoter) is not reduced to practice until the inventor can define it by "its physical or chemical properties" (e.g. a DNA sequence).

Given the claim breadth and lack of description as discussed above, the specification fails to provide an adequate written description of the genus of sequences as broadly claimed. Given the lack of written description of the claimed genus of sequences, any method of using them, such as transforming plant cells and plants therewith, and the resultant products including the claimed transformed plant cells and plants containing the genus of sequences, would also be inadequately described. Accordingly, one skilled in the art would not have recognized Applicant to have been in possession of the claimed invention at the time of filing. See the Written Description

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Requirement guidelines published in Federal Register/ Vol. 66, No. 4/ Friday January 5, 2001/ Notices: pp. 1099-1111.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-3, 19, 25, 30, 40, 44-46, 54, 56-60, 66-67, 76, 82 and 96 are rejected under 35 U.S.C. 102(b) as being anticipated by Preuss et al (US Patent 6156953, published 12/05/2000).

Claims 1-3 and 96 are drawn to a plant comprising a mini-chromosome wherein said mini-chromosome has a transmission efficiency of 80%, 90% or 95% during mitotic and meiotic division respectively.

Claims 19, 25, and 30 are drawn to the above plant comprising the mini-chromosome wherein the mini-chromosome comprises an exogenous nucleic acid operably linked to a regulatory element and confers herbicide, insect, disease or stress resistance.

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Claims 40, and 43-44, are drawn to the plant comprising a mini-chromosome wherein the mini-chromosome comprises a repeated nucleotide sequence wherein the sequence is repeated at least 5 times, a telomere and wherein the mini-chromosome is circular.

Claims 45-46, 54, and 56-60 are drawn to a plant comprising a mini-chromosome wherein the plant is a monocot or a dicot, a meicyote, gamete, ovule, pollen or endosperm of said plant, a seed, embryo or propagule of said plant, a progeny of said plant, wherein the progeny is a result of self breeding or cross breeding.

Claims 66-67, 76 and 82 are drawn to methods of making a mini-chromosome and making a plant, respectively, comprising identifying a centromere nucleotide sequence in a genomic DNA library using a multiplicity of diverse probes and constructing a mini-chromosome comprising the centromere nucleotide sequence wherein at least one probe hybridizes to arrays of tandem repeats in genomic DNA, and a method of making a plant comprising delivering a mini-chromosome using a biolistic method.

Preuss et al teach a plant transformed with an artificial chromosome wherein the segregation is stable, which inherently is greater than the currently claimed 95%, 90% or 80% transmission efficiency (see 1st paragraph under Summary of Invention, claims 1, 6, 18-19, and 21-27, for example), wherein the artificial chromosome comprises an herbicide resistant gene operably linked to a regulatory element (See Heading XVII Exogenous Genes for Expression in plants, 3rd paragraph, for example and claims 23-26), wherein the artificial chromosome comprises a telomere (see claims 18-19), the

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pAL1 repeat (a repeated nucleotide sequence that is repeated at least 5 times, see paragraph 6 under Detailed Description of the Invention and wherein a large portion of the mapped centromere makes up the recombinant construct inherently comprising 5 or more repeats) wherein the chromosome is circular (see paragraph 3 under the heading VI. PLAC constructs, for example), wherein transformation is carried out biolistically (see part ii under XV. Transformed Host Cells and Transgenic Plants, for example) wherein the plant may be a monocot or dicot (see paragraph 5 under Definitions, for example, and paragraph 6 under Summary of Invention, for example), a propagule, ovule, or seed therefrom (see in particular paragraph 6 under iii Environment or Stress Resistance wherein the specification states "For example, expression of genes that improve the synchrony of pollen shed and receptiveness of the female flower parts, i.e., silks, would be of benefit") and progeny resulting from self crossing or out crossing (see 7th paragraph under iii Agrobacterium-Mediated Transfer, for example), and methods of making a minichromosome and a plant (see claims, for example), wherein a multiplicity of probes are used to identify the centromere (see Examples 3-5, for example).

Claims 1-3, 7, 10-11, 14-16, 19, 25, 30, 43-46, 54, 57-58, 63, 66-67, 76-77, 82-83 and 96 are rejected under 35 U.S.C. 102(e) as being anticipated by Luo et al (US20020123053).

Claims 1-3 and 96 are drawn to a plant comprising a mini-chromosome wherein said mini-chromosome has a transmission efficiency of 80%, 90% or 95% during mitotic and meiotic division respectively.

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Claim 7 is drawn to the above wherein the minichromosome is 1000 kb or less.

Claim 10 is drawn to the above wherein the minichromosome comprises a site for site-specific recombination.

Claim 11 is drawn to plant comprising a minichromosome comprising a centromere derived from a crop plant centromere.

Claim 14 is drawn to a plant comprising a minichromosome wherein the centromere comprises an artificially synthesized repeated sequence.

Claims 15-16 are drawn to a plant comprising a minichromosome any nucleotide may be inserted relative to the donor centromere and wherein the minichromosome is passaged through one or more hosts.

Claims 19, 25, and 30 are drawn to the above plant comprising the mini-chromosome wherein the mini-chromosome comprises an exogenous nucleic acid operably linked to a regulatory element and confers herbicide, insect, disease or stress resistance.

Claims 40, and 43-44, are drawn to the plant comprising a mini-chromosome wherein the mini-chromosome comprises a repeated nucleotide sequence wherein the sequence is repeated at least 5 times, a telomere and wherein the mini-chromosome is circular.

Claims 45-46, 54, and 56-58 are drawn to a plant comprising a mini-chromosome wherein the plant is a monocot or a dicot, a seed, embryo or propagule of said plant, or a progeny of said plant.

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Claim 63 is drawn to the above progeny wherein the centromere is less than 150 kb in length.

Claims 66-67, 76-77 and 82-83 are drawn to methods of making a mini-chromosome and making a plant, respectively, comprising identifying a centromere nucleotide sequence in a genomic DNA library using a multiplicity of diverse probes and constructing a mini-chromosome comprising the centromere nucleotide sequence wherein at least one probe hybridizes to arrays of tandem repeats in genomic DNA, and a method of making a plant comprising delivering a mini-chromosome using a biolistic method and wherein at least one probe hybridizes to ribosomal DNA and wherein the liquid from biolistic transformation comprises a divalent ion and a di-or poly-amine.

Luo et al teaches a plant transformed with a minichromosome (see claims 1, 12-13, 34-40, 56, 60-62, 67-71, 74, 91-97, 103-105, 109, 113-116 and 119), wherein the segregation efficiency (which is the same as transmission efficiency) is 80%, 90% or 95% (see paragraph 231 under Definitions of centromere nucleic acid sequence) wherein the mini chromosomes is less than 1000kb (see paragraph 45 where the centromere is estimated to be about 100 kb, and the combined additional elements are less than 100kb see paragraph 190 for telomere and 191 for ARS), and comprising a site-specific recombination site (see Figure 11, for example), wherein the minichromosome is passaged through at least one host (see claim 119 including progeny) a selectable marker (see claims and paragraph 193) including herbicide resistance, an artificially synthesized repeat (see paragraph 188) wherein the centromere repeat number is at least 5 (see paragraph 107) wherein the

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minichromosome is circular (see paragraph 195, for example), wherein the plant is monocot or dicot (see claims recited above, for example), progeny (see claim 119) or seed (see paragraph 137, for example), methods of making a minichromosome and plant, respectively, comprising identifying a centromere (see recited claims above, for example) using a multiplicity of diverse probes (see paragraph 107, for example), delivering using a biolistic method (see paragraphs 144-149, for example), wherein at least one probe hybridizes to ribosomal DNA (see Figures 4A and 4B as well as Example 2, for example) and wherein the liquid from the biolistic transformation comprises a divalent ion and a di- or poly-amine (see paragraph 95, for example and reference materials on biolistic transformation, for example).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Claims 1-3, 10-11, 15-16, 19, 25, 30, 40, 43-46, 54, 56-58, 66-67, 76, 82, 89-90, 93, and 96 are rejected under 35 U.S.C. 102(e) as being anticipated by Keith et al (US Patent 7119250, filed 06/12/2002).

The claims are drawn to plants comprising minichromosomes, wherein said minichromosome has a transmission efficiency of 80%, 90% or 95% during mitotic and

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meiotic division respectively wherein the minichromosome comprises a centromere nucleic acid sequence wherein there are at least 5 repeats of the centromere repeat, wherein the centromere is derived from a commercial crop plant wherein the mini-chromosome comprises an exogenous nucleic acid operably linked to a regulatory element and confers herbicide, insect, disease or stress resistance, wherein the plant is a monocot or a dicot, a seed, embryo or propagule of said plant, or a progeny of said plant and methods of making a mini-chromosome and making a plant, respectively, comprising identifying a centromere nucleotide sequence in a genomic DNA library using a multiplicity of diverse probes and constructing a mini-chromosome comprising the centromere nucleotide sequence wherein at least one probe hybridizes to arrays of tandem repeats in genomic DNA, and a method of making a plant comprising delivering a mini-chromosome using a biolistic method.

Keith et al teach a plant comprising a minichromosome wherein the plant is a dicot or monocot (see paragraph 13 under summary of Invention, for example), wherein the plant and centromeric sequence are from a commercial crop (see claims 4-6 and 15-22, for example) wherein the centromere repeat is at least 5 copies (see claim 1, for example), progeny from said plant (see claim 29), a plant part (see claim 32), wherein the minichromosome comprises an exogenous nucleic acid operably linked to a regulatory sequence wherein the nucleic acid is an herbicide resistance gene, or an insect resistance gene (see section X as well as claim 3, for example) and methods for identifying centromeres using a multiplicity of probes (see section IV, for example).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-3, 7, 10-11, 14-16, 19, 25, 30, 39-40, 43-46, 54, 56-63, 66-67, 76-77, 82-83, 89-90, 93 and 96 are rejected under 35 U.S.C. 103(a) as being unpatentable over Preuss et al (US Patent 6156953, published 12/05/2000), in view of Luo et al (US20020123053)

Claims 1-3, 19, 25, 30, 40, 43-46, 54, 56-60, 66-67, 76, 82 and 96 are rejected as being obvious over Preuss et al as applied above.

Claims 7, 10-11, 14-16, 39, 61-63, 77, 83, 89-90 and 93 are further rejected as being obvious over Preuss et al in view of Luo et al.

Claims 1-3 and 96 are drawn to a plant comprising a mini-chromosome wherein said mini-chromosome has a transmission efficiency of 80%, 90% or 95% during mitotic and meiotic division respectively.

Claim 7 is drawn to the above wherein the minichromosome is 1000 kb or less.

Claim 10 is drawn to the above wherein the minichromosome comprises a site for site-specific recombination.

Claim 11 is drawn to plant comprising a minichromosome comprising a centromere derived from a crop plant centromere.

Claim 14 is drawn to a plant comprising a minichromosome wherein the centromere comprises an artificially synthesized repeated sequence.

Claims 15-16 are drawn to a plant comprising a minichromosome any nucleotide may be inserted relative to the donor centromere and wherein the minichromosome is passed through one or more hosts.

Claims 19, 25, and 30 are drawn to the above plant comprising the mini-chromosome wherein the mini-chromosome comprises an exogenous nucleic acid operably linked to a regulatory element and confers herbicide, insect, disease or stress resistance.

Claim 39 is drawn to the above wherein the number of repeated copies of the repeated sequence are less than 1000.

Claims 40, and 43-44, are drawn to the plant comprising a mini-chromosome wherein the mini-chromosome comprises a repeated nucleotide sequence wherein the sequence is repeated at least 5 times, a telomere and wherein the mini-chromosome is circular.

Claims 45-46, 54, and 56-58 are drawn to a plant comprising a mini-chromosome wherein the plant is a monocot or a dicot, a seed, embryo or propagule of said plant, or a progeny of said plant.

Claims 61-63 are drawn to the progeny above wherein the progeny is a result of apomixes, clonal propagation and wherein the centromere is less than 150 kilobases in length.

Claims 66-67, 76-77 and 82-83 are drawn to methods of making a mini-chromosome and making a plant, respectively, comprising identifying a centromere nucleotide sequence in a genomic DNA library using a multiplicity of diverse probes and constructing a mini-chromosome comprising the centromere nucleotide sequence wherein at least one probe hybridizes to arrays of tandem repeats in genomic DNA, and a method of making a plant comprising delivering a mini-chromosome using a biolistic method and wherein at least one probe hybridizes to ribosomal DNA and wherein the liquid from biolistic transformation comprises a divalent ion and a di-or poly-amine.

Claims 89-90 and 93 are drawn to methods of using the plant of claim 1 to produce a food product a recombinant protein or a chemical product, respectively.

Preuss et al teach a plant transformed with an artificial chromosome wherein the segregation is stable, which inherently is greater than the currently claimed 95%, 90% or 80% transmission efficiency (see 1st paragraph under Summary of Invention, claims 1, 6, 18-19, and 21-27, for example), wherein the artificial chromosome comprises an herbicide resistant gene operably linked to a regulatory element (See Heading XVII Exogenous Genes for Expression in plants, 3rd paragraph, for example and claims 23-26), wherein the artificial chromosome comprises a telomere (see claims 18-19), the pAL1 repeat (a repeated nucleotide sequence that is repeated at least 5 times, see paragraph 6 under Detailed Description of the Invention and wherein a large portion of the mapped centromere makes up the recombinant construct inherently comprising 5 or more repeats) wherein the chromosome is circular (see paragraph 3 under the heading VI. PLAC constructs, for example), wherein transformation is carried out biolistically

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(see part ii under XV. Transformed Host Cells and Transgenic Plants, for example) wherein the plant may be a monocot or dicot (see paragraph 5 under Definitions, for example, and paragraph 6 under Summary of Invention, for example), a propagule, ovule, or seed therefrom (see in particular paragraph 6 under iii Environment or Stress Resistance wherein the specification states "For example, expression of genes that improve the synchrony of pollen shed and receptiveness of the female flower parts, i.e., silks, would be of benefit") and progeny resulting from self crossing or out crossing (see 7th paragraph under iii Agrobacterium-Mediated Transfer, for example), and methods of making a minichromosome and a plant (see claims, for example), wherein a multiplicity of probes are used to identify the centromere (see Examples 3-5, for example).

Preuss et al do not teach wherein the minichromosome is 1000 kb or less, wherein the minichromosome comprises a site for site-specific recombination, wherein the plant comprising a minichromosome comprises a centromere derived from a crop plant centromere, wherein the centromere comprises an artificially synthesized repeated sequence, wherein the minichromosome is passaged through one or more hosts, wherein the number of repeated copies of the repeated sequence are less than 1000, wherein the progeny is a result of apomixes, clonal propagation and wherein the centromere is less than 150 kilobases in length. Preuss et al do not teach methods of making a mini-chromosome and making a plant, respectively, comprising identifying a centromere nucleotide sequence in a genomic DNA library using a multiplicity of diverse probes wherein at least one probe hybridizes to ribosomal DNA and wherein the liquid from biolistic transformation comprises a divalent ion and a di-or poly-amine. Preuss et

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al do not teach methods of using the plant of claim 1 to produce a food product a recombinant protein or a chemical product, respectively.

Luo et al teaches a plant transformed with a minichromosome (see claims 1, 12-13, 34-40, 56, 60-62, 67-71, 74, 91-97, 103-105, 109, 113-116 and 119), wherein the segregation efficiency (which is the same as transmission efficiency) is 80%, 90% or 95% (see paragraph 231 under Definitions of centromere nucleic acid sequence) wherein the mini chromosomes is less than 1000kb (see paragraph 45 where the centromere is estimated to be about 100 kb, and the combined additional elements are less than 100kb see paragraph 190 for telomere and 191 for ARS), and comprising a site-specific recombination site (see Figure 11, for example), wherein the minichromosome is passaged through at least one host (see claim 119 including progeny) a selectable marker (see claims and paragraph 193) including herbicide resistance, an artificially synthesized repeat (see paragraph 188) wherein the centromere repeat number is at least 5 (see paragraph 107) wherein the minichromosome is circular (see paragraph 195, for example), wherein the plant is monocot or dicot (see claims recited above, for example), progeny (see claim 119) or seed (see paragraph 137, for example), methods of making a minichromosome and plant, respectively, comprising identifying a centromere (see recited claims above, for example) using a multiplicity of diverse probes (see paragraph 107, for example), delivering using a biolistic method (see paragraphs 144-149, for example), wherein at least one probe hybridizes to ribosomal DNA (see Figures 4A and 4B as well as Example 2, for example) and wherein the liquid from the biolistic transformation

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comprises a divalent ion and a di- or poly-amine (see paragraph 95, for example and reference materials on biolistic transformation, for example).

Given the state of the art and disclosures by Preuss et al and Luo et al, it would have been obvious to use the centromere compounds identified by Luo et al and use them in the construct taught by Preuss et al as suggested by Luo et al wherein Luo et al suggest both interchangeable centromeres from different crop species, but also demonstrate the constructs in Arabidopsis, the plant exemplified by Preuss et al. All of the elements of the instant invention are known elements. Furthermore, methods for producing food, recombinant proteins, and chemicals by using transgenic plants are well known in the art. The artificial chromosomes of the instant invention represent a vector that could be utilized for the same common uses of the vectors used in the prior art including food, recombinant protein, and chemical production.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to

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be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-3, 19, 25, 30, 40, 43-46, 54, 56-60, 66-67, 76, 82 and 96 are rejected on the ground of nonstatutory double patenting over claims 1, 2, 6, 17-19, 21-24 and 25-27 of U. S. Patent No. 6156953 since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter, as follows: Both the issues patent and instant invention are claiming plants or plant cells comprising a minichromosome wherein the minichromosome comprises a plant centromere, telomere and ARS sequence and further comprising a gene of interest and selectable marker. The claims as currently written encompass the claims of the issued patent.

Furthermore, there is no apparent reason why applicant was prevented from presenting claims corresponding to those of the instant application during prosecution of the application which matured into a patent. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

Claims 1-3, 19, 25, 30, 40, 43-46, 66-67, 76, 82 and 96 are rejected on the ground of nonstatutory double patenting over claims 1-4 and 8-13 of U. S. Patent No.

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6900012 since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter, as follows: Both the issues patent and instant invention are claiming plants or plant cells comprising a minichromosome wherein the minichromosome comprises a plant centromere, telomere and ARS sequence and further comprising a gene of interest and selectable marker. The claims as currently written encompass the claims of the issued patent.

Furthermore, there is no apparent reason why applicant was prevented from presenting claims corresponding to those of the instant application during prosecution of the application which matured into a patent. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

Claims 1-3, 10-11, 15-16, 19, 25, 30, 40, 43-46, 54, 56-58, 66-67, 76, 82, 89-90, 93, and 96 are rejected on the ground of nonstatutory double patenting over claims 1-38 of U. S. Patent No. 7119250 since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter, as follows: Both the issues patent and instant invention are claiming plants or plant cells comprising a minichromosome wherein the

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minichromosome comprises a plant centromere, telomere and ARS sequence and further comprising a gene of interest and selectable marker. The claims as currently written encompass the claims of the issued patent.

Furthermore, there is no apparent reason why applicant was prevented from presenting claims corresponding to those of the instant application during prosecution of the application which matured into a patent. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

Claims 1-3, 19, 25, 30, 40, 43-46, 66-67, 76, 82 and 96 are rejected on the ground of nonstatutory double patenting over claims 1-16 of U. S. Patent No. 7015372 since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter, as follows: Both the issued patent and instant invention are claiming plants or plant cells comprising a minichromosome wherein the minichromosome comprises a plant centromere, telomere and ARS sequence and further comprising a gene of interest and selectable marker. The claims as currently written encompass the claims of the issued patent.

Furthermore, there is no apparent reason why applicant was prevented from presenting claims corresponding to those of the instant application during prosecution of

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the application which matured into a patent. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

Claims 1-3, 11, 15-16, 19, 25, 30, 40, 43-44, 46, 54, 56-58, and 96 are rejected on the ground of nonstatutory double patenting over claims 1-7 of U. S. Patent No. 7235716 since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter, as follows: Both the issues patent and instant invention are claiming plants or plant cells comprising a minichromosome wherein the minichromosome comprises a plant centromere, telomere and further comprising a gene of interest and selectable marker. The claims as currently written encompass the claims of the issued patent.

Furthermore, there is no apparent reason why applicant was prevented from presenting claims corresponding to those of the instant application during prosecution of the application which matured into a patent. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

Claims 1-3, 11, 15-16, 19, 25, 30, 40, 43-44, 46, 54, 56-58, and 96 are rejected on the ground of nonstatutory double patenting over claims 1-7 of U. S. Patent No.

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7227057 since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter, as follows: Both the issues patent and instant invention are claiming plants or plant cells comprising a minichromosome wherein the minichromosome comprises a plant centromere, telomere and further comprising a gene of interest and selectable marker. The claims as currently written encompass the claims of the issued patent.

Furthermore, there is no apparent reason why applicant was prevented from presenting claims corresponding to those of the instant application during prosecution of the application which matured into a patent. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

Claims 1-3, 7, 10-11, 14-16, 19, 25, 30, 40, 43-44, 46, 54, 56-58, 66-67, 76-77 and 96 are rejected on the ground of nonstatutory double patenting over claims 1-22 of U. S. Patent No. 7226782 since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter, as follows: Both the issues patent and instant invention are claiming plants or plant cells comprising a minichromosome wherein the

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minichromosome comprises a plant centromere, telomere and further comprising a gene of interest and selectable marker. The claims as currently written encompass the claims of the issued patent.

Furthermore, there is no apparent reason why applicant was prevented from presenting claims corresponding to those of the instant application during prosecution of the application which matured into a patent. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

Claims 1-3, 7, 10-11, 14-16, 19, 25, 30, 40, 43-45, 54, 56-58, 66-67, 76-77, 89-90, 93 and 96 are rejected on the ground of nonstatutory double patenting over claims 1-22 of U. S. Patent No. 7456013 since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter, as follows: Both the issued patent and instant invention are claiming plants or plant cells comprising a minichromosome wherein the minichromosome comprises a plant centromere, telomere and further comprising a gene of interest and selectable marker. The claims as currently written encompass the claims of the issued patent.

Furthermore, there is no apparent reason why applicant was prevented from presenting claims corresponding to those of the instant application during prosecution of

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the application which matured into a patent. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

Claims 1-3, 7, 11, 19, 25, 30, 39-40, 43-46, 66-67 and 96 are provisionally rejected on the ground of nonstatutory double patenting over claims 128-129, 132-145 and 150-152 of copending Application No. 11981296. This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

The subject matter claimed in the instant application is fully disclosed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application and the instant application are claiming common subject matter, as follows: Both the issues patent and instant invention are claiming plants or plant cells comprising a minichromosome wherein the minichromosome comprises a plant centromere, telomere and further comprising a gene of interest and selectable marker. The claims as currently written encompass the claims of the copending application.

Furthermore, there is no apparent reason why applicant would be prevented from presenting claims corresponding to those of the instant application in the other copending application. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

Claims 1-3, 7, 11, 19, 25, 30, 39-40, 43-46, 56-58, 66-67 and 96 are provisionally rejected on the ground of nonstatutory double patenting over claims 128-133, 135-147

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of copending Application No. 11981451. This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

The subject matter claimed in the instant application is fully disclosed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application and the instant application are claiming common subject matter, as follows: Both the issues patent and instant invention are claiming plants or plant cells comprising a minichromosome wherein the minichromosome comprises a plant centromere, telomere and further comprising a gene of interest and selectable marker. The claims as currently written encompass the claims of the copending application.

Furthermore, there is no apparent reason why applicant would be prevented from presenting claims corresponding to those of the instant application in the other copending application. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

Claims 1-3, 19, 25, 30, 40, 43-46, 56-58, and 96 are provisionally rejected on the ground of nonstatutory double patenting over claims 1-2, 7-8, 14, 18, 24, 30, 55-56 and 59 of copending Application No. 11331942. This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

The subject matter claimed in the instant application is fully disclosed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application and the instant

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application are claiming common subject matter, as follows: Both the issues patent and instant invention are claiming plants or plant cells comprising a minichromosome wherein the minichromosome comprises a plant centromere, telomere and further comprising a gene of interest and selectable marker. The claims as currently written encompass the claims of the copending application.

Furthermore, there is no apparent reason why applicant would be prevented from presenting claims corresponding to those of the instant application in the other copending application. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BRENT PAGE whose telephone number is (571)272-5914. The examiner can normally be reached on Monday-Friday 8-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on (571)-272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Brent T Page

/Anne Marie Grunberg/
Supervisory Patent Examiner, Art Unit 1638